Comparative Toxicity of Gasoline Oxygenates

by

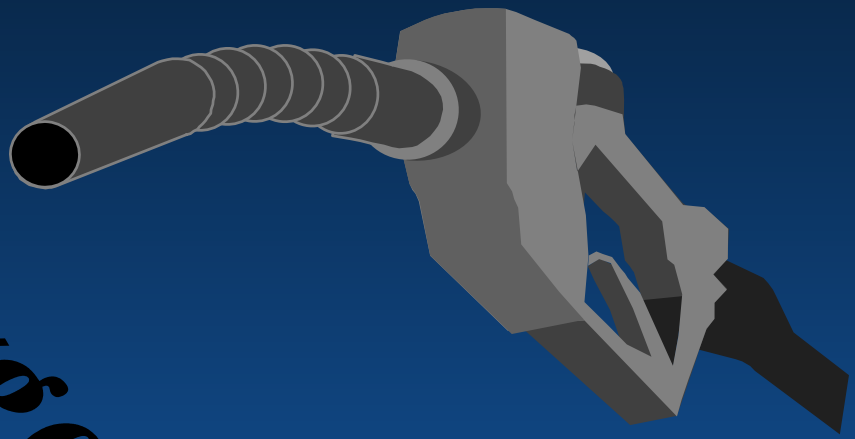
Heriberto Robles, Ph.D., D.A.B.T.

and

Teri L. Copeland, M.S., D.A.B.T.

September 25, 2002

Oxygenates in Gasoline



- Brief History
- Environmental Benefits
- MTBE Phased Out of CA
- Comparative Toxicity
- Alternatives

CAAA (1990) Mandates

- ✓ 1992: Gasoline with 2.7% O_2 nonattainment areas
- ✓ EtOH, MeOH, MTBE, ETBE, TAME, DIPE, TBA
- ✓ MTBE preferred option

Air Quality Benefits in CA

- ✓ = Removing 3.5 million (old) cars
- ✓ ⬇ 1,300 tons CO/day; 20 tons benzene/day
- ✓ ⬇ Tailpipe emissions of air toxics
- ✓ ⬇ Cancer risk by 40% or 60/million

Air Quality Benefits (cont.)

- ✓ South Coast Air Basin
  - Ozone levels ⇩ 18% in 1996 vs. 94-95
- ✓ Sacramento
  - Ozone ⇩ 12%
- ✓ Southern California
  - Ozone ⇩ 10%

MTBE in Groundwater

Santa Monica (4/1996)

- **3 municipal drinking water wells**
- **Suspected - LUSTs**
- **MTBE at 590 ug/L**

MTBE Phased Out of California

- "There is a significant risk to the environment from using MTBE in gasoline in California"
- CARB to lower or remove O_2 content requirement
- Evaluate ethanol as an alternative

Gasoline Oxygenates

EtOH, MeOH, MTBE, ETBE, TAME, DIPE, TBA

TAEE, THxME, THpME, THxEE, THpEE, DME, etc.

Alternatives Must:

- ✓ Attain air quality benefits
- ✓ Less mobile and persistant in sub-soil
- ✓ Have an extensive toxicological database
- ✓ Less toxic than MTBE, and
- ✓ Have less offensive odor

Water Solubility

MTBE	5.0 g/100 ml
EtOH	Miscible
MeOH	Miscible
TBA	Miscible
ETBE	<0.1g/100 ml
TAME	No information
DIPE	0.88 g/100 ml

Biodegradation

MTBE	Resistant to degradation
EtOH	Biodegradable (urethane?)
MeOH	Formic acid
TBA	Biodegradable
ETBE	No information
TAME	No information
DIPE	Resistant

Half-life in Water

MTBE	4 hours to 4 days
EtOH	6 days
MeOH	5 to 52 days
TBA	2.2 to 129 days
ETBE	No information
TAME	No information
DIPE	3 hours to 4 days

Half-life in Air

MTBE	5.5 to 50 days
EtOH	Hours to 6 days
MeOH	18 days
TBA	14.7 days
ETBE	No information
TAME	No information
DIPE	21 hours

Odor

MTBE	Sharp, ether-like
EtOH	Pleasant alcoholic
MeOH	Pleasant alcoholic
TBA	Camphor-like
ETBE	No information
TAME	No information
DIPE	Pungent, ether-like

Comparative Toxicity

Why ?

- **Risk = Exposure x Toxicity**
- **Maximum Air Benefits**
- **Minimum Environmental and Health Risks**
- **Risk Assessment of Past Releases**
- **Maximize Existing (Incomplete) Databases**

Toxicity Assessment

- Dose-Response
- Systemic Toxicity / Neurotoxicity
- Reproductive/ Developmental Toxicity
- Carcinogenicity
- Metabolism

MTBE Toxicity

- ✓ Target organs: kidney and liver
- ✓ Toxic doses ➲ tumors
  - Chronic cell damage
  - No cancer at tolerable doses
  - Studies had technical limitations
  - Cancers seen are rodent specific
  - MTBE not genotoxic
- ✓ Not a human carcinogen (IARC, 1998)

Carcinogenicity Bioassays:

MTBE			
Chun et al, 1992	F-344 rat	Inhalation	400, 3000, 8000 ppm
Belpoggi et al, 1995	Sprague Dawley rat	Oral (oil)	250, 1000 mg/kg
Burleigh-Flayer et al, 1992	CD-1 mouse	Inhalation	400, 3000, 8000 ppm
Bird et al, 1997	F-344 rat CD-1 mouse	Inhalation	400, 3000, 8000 ppm
TBA			
Cirvelli et al, 1995	F-344 rat B6C3F mouse	Oral Drinking Water	1,25, 2.5, 5 mg/L 5,10,20 mg/L

Carcinogenicity: Liver

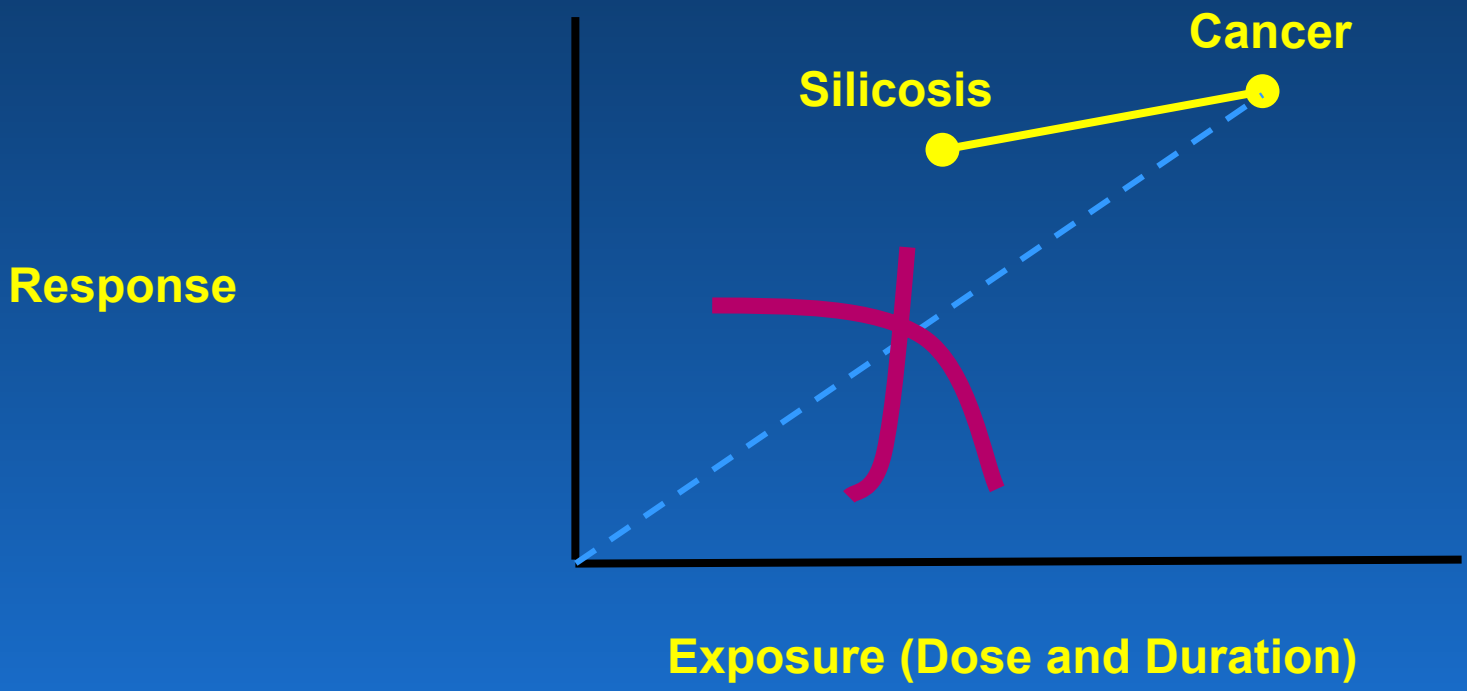
TBA (Oral, rat & mouse)

- None up to 5 mg/L

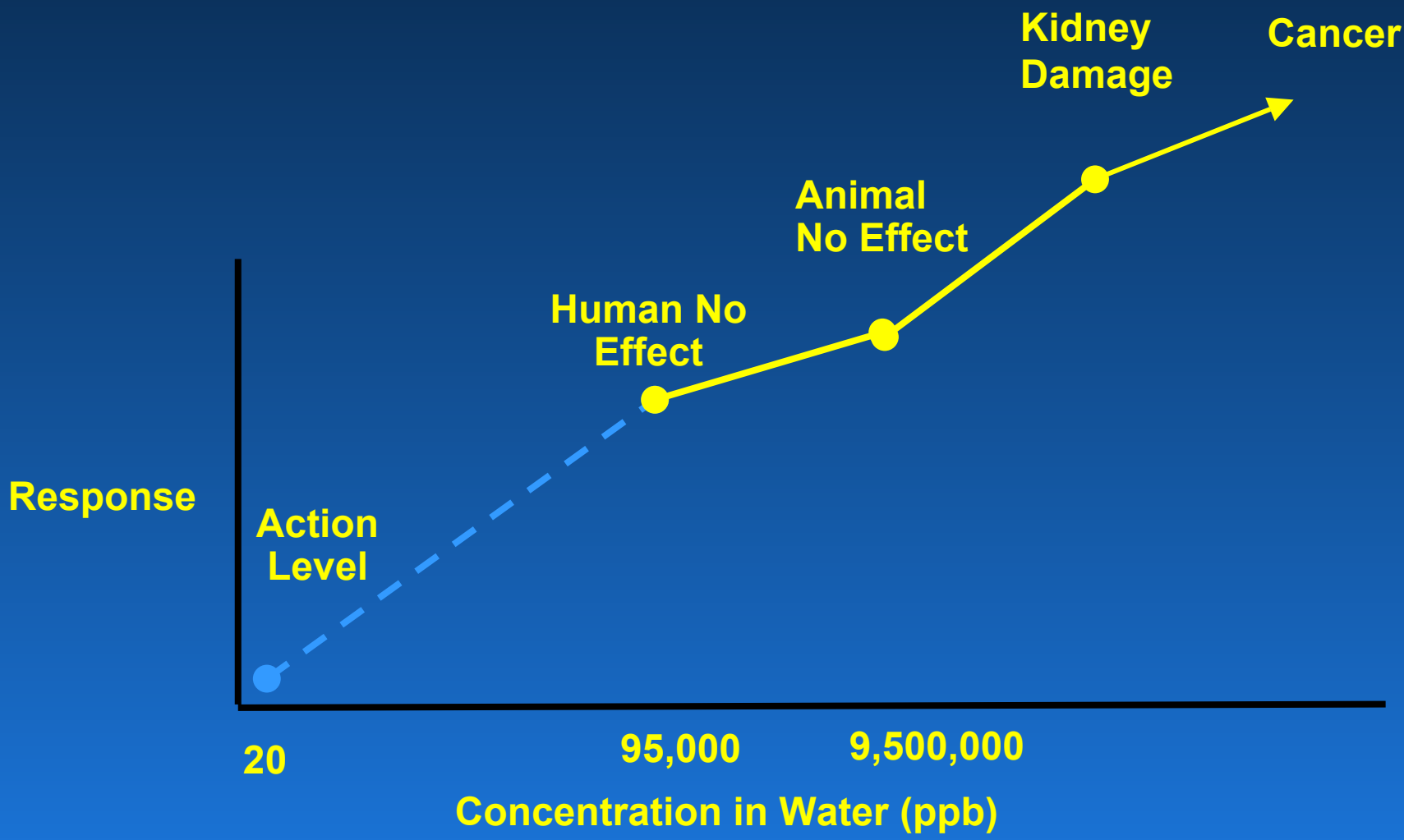
MTBE

- Female Mice Only (inhalation only)
- > MTD (8,000 ppm), Weak Response
- Tumor 2^0 to Toxic Response
- Increase in Cell Division, Classic Mechanism (sand, alcohol)
- Consensus (incl. CalEPA) not Relevant to Humans

Example: Respirable Silica



Example: MTBE



Carcinogenicity: Thyroid

TBA (Oral, rat & mouse)

- Mouse - > MTD (20 mg/L)

MTBE (mouse)

- > MTD (8,000 ppm), Weak Response

*Tumor 2^0 to Toxic Response

*Increase in Cell Division, Classic Mechanism (alcohol, phenobarbitol)

*Consensus (incl. CalEPA) not Relevant to Humans

Carcinogenicity: Lymphomas and Leukemias

TBA (Oral, rat & mouse)

- None up to 5 mg/L

MTBE

- Female Rat Only (oral gavage only)
- > MTD Only
- Statistically Significant Only if Summed
- Generally Inappropriate to Sum (NTP, 1986)
- Summed Data Used by CalEPA as basis for CPF/PHG

Carcinogenicity : Testicular Tumors

TBA (Oral, rat & mouse)

- None up to 5 mg/L

MTBE

- Male Rat Only (inhalation, oral gavage)
- ≥ MTD (8000 ppm) Only, Weak Response
- High Background Rate in Lab Rodents
- Decreased Survival in Study Controls
- Not Significant With NTP Control Data
- Used as Basis for CalEPA CPF/PHG

Carcinogenicity: Kidney Tumors

TBA (Oral, rat & mouse)

- Rat – Weak Response at High Dose (5 mg/L)

MTBE

- Male Rat Only (inhalation only)
- Weak Response at 3,000 and 8,000 ppm (lethal doses)
- USEPA, IARC, HEI, NRC Tumors Not Relevant to Humans
- CalEPA disagrees
- Study used as basis for CalEPA CPF/PHG

MTBE - Weight-of-Evidence for Cancer

- Carcinogenic Potential for Humans is Very Low
- No Epidemiological Evidence of Cancer
- Rodent Tumors Elevated Only at Doses >> MTD
- Rodent Tumors Only After Chronic Progressive Cytotox
- Not Genotoxic (threshold)
- Tumor Mechanisms Species-Specific
- Human Health Risk Additionally Deemed Low Based on Offensive Odor at Low Levels
- USEPA, IARC, WHO, ATSDR Classify as Animal Carcinogen
- CalEPA Classifies as Carcinogen (not listed by Prop 65)

Ethyl Alcohol (EtOH)

- ✓ Most studied chemical
- ✓ CNS, liver, kidney, cardiovascular, gastrointestinal, endocrine
- ✓ Teratogen, co-carcinogen, reproductive toxicant
- ✓ No health risks expected when mixed with gasoline

Methyl Alcohol (MeOH)

- ✓ Widely studied due to intentional, accidental and occupational exposure
- ✓ CNS, metabolic acidosis, eyes, male reproductive organs
- ✓ Teratogen and fetotoxic
- ✓ Limited info. on low-level, chronic exposure

tertiary-Butyl Alcohol (TBA)

- ✓ 2 to 5 times more toxic than EtOH
- ✓ Kidney effects similar to MTBE
- ✓ CNS, liver, kidney and cardiac damage
- ✓ Not classifiable as a human carcinogen

Ethyl tert-Butyl Ether (ETBE)

- ✓ Very limited information
- ✓ Structurally not likely to be genotoxic and carcinogen

Diisopropyl ether (DIPE)

- ✓ $1^1/_2$ - 2 times more toxic than ethyl ether
- ✓ CNS depression, anesthesia, death
- ✓ Few injuries and death from industrial exposure
- ✓ May produce liver and brain damage (chronic)
- ✓ May be teratogenic

tert-Amyl Methyl Ether (TAME)

- ✓ Limited information
- ✓ More severe CNS depression than that resulting from MTBE exposure
- ✓ May be teratogen and mutagen

Conclusions

- Benefits outweigh risks (?)
- MTBE best oxygenate (?)
- MeOH second best (?)
- Increased control of soil and groundwater releases
- Risk-based cleanup programs

Regulatory Criteria

MTBE:	CalEPA	USEPA	ATSDR
Acceptable Dose (mg/kg-d)	2.29	0.857	Acute: 0.4 Intermed. 0.3
Acceptable Air Concentration	0.001 ppm (ca, air PRG IX)	0.869 ppm (air PRG IX)	Acute: 2 ppm Int/Chronic: 0.7 ppm
Cancer Slope Factor (mg/kg-d) -1	0.0018	none	none
Public Health Goal (H20)	13 ppb (ug/L)	NA	NA
Primary MCL	none	none	NA
Secondary MCL	5 ppb (odor/taste)	none	NA
USEPA Drinking Water Advisory		20-40 ppb (odor/taste)	
DHS Interim Action Level	35 ppb (odor)		
DHS Proposed New Limit (regulation)	5 ppb (odor, taste)		
TBA: Michigan 550 ppb Drink. water guideline			